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FLOATING BILAYER TABLET: A REVIEW ON FORMULATION STATERGIES, EVALUATION METHODS AND PHARMACEUTICAL APPLIACATION

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Abstract:
Floating drug delivery systems (FDDS) are included in the category of gastro-retentive drug delivery systems (GRDDS). By enhancing the drug's buoyancy over stomach fluids, Longer medicine half-lives are made possible by the floating drug delivery system (FDDS). When added to GRDDS, medications that are less soluble in high pH conditions have increased bioavailability and solubility. Drugs with a limited GIT absorption window make excellent candidates for floating drug delivery systems. It works better to treat local infections of the gastrointestinal tract in addition to systemic usage In order to compile the most recent research on floating drug delivery systems (FDDS), this review was created with a focus on the primary mechanism of flotation to achieve stomach retention. The review seeks to give FDDS a general overview., or floating bilayer, including its mechanism, the many technologies needed for its manufacture, a summary of its characterization, and the in vivo performance of GRDDS.

Keyword: Bilayer floating tablet, floating drug delivery system, mechanism , advantage and disadvantage, factor affecting , classification , method and evaluation, recent work on floating bilayer tablet.

Introduction

As a first step toward reducing chemical incompatibilities of API through separation (physical separation), bilayer floating tablets allow for the creation of various drug release options, including prolonged and quick release . Because floating DDS has a lower bulk density than GIT fluids, it will concentrate and float in stomach fluid without interfering with the GIT emptying rate over an extended length of time. The medication is released sluggishly at the necessary pace and consistently afloat on the surface of the food while the system is buoyant on the gastric fluid (GI fluid).[1]

By physically separating the ingredients, bilayer tablets can be used to produce different medication release profiles (immediate release with prolonged release) and avoid chemical

incompatibilities across API. The mechanical structures of this drug delivery system are extremely challenging, despite its benefits, due to the use of numerous materials and intricate geometric boundaries between the layers. The development of advanced tablet forms and patient-friendly administration presents several challenges for pharmaceutical scientists and engineers.[2]

The bilayer tablet is a far superior approach than the one-layer tablet. Bilayer tablets instant release layer distributes the first dose and includes super disintegrates, which quickens the drug's rate of release and makes it start working right away (a loading dose). By employing a range of polymers as release retardants, the sustained release (maintenance dosage) layer, in contrast, releases the medication gradually over an extended period of time.. Drugs that are diabetic, antihypertensive, antihistamine, analgesic, antipyretic, and antiallergenic(allergy-free) are generally appropriate for this kind of delivery.[3]

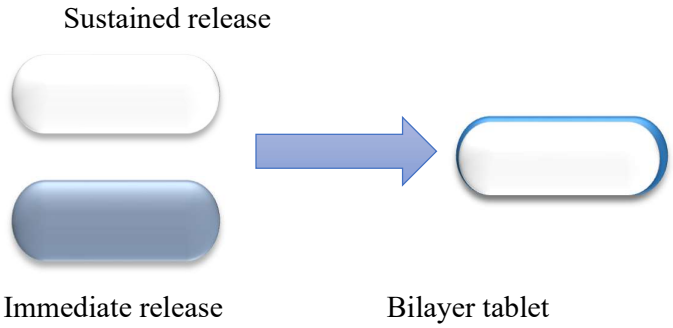


Fig 1 Bilayer tablet

Drug delivery system that floats FDDS is a member of the class of gastro-retentive dosage forms that Davis (1968) first identified. With a longer time for the release of active pharmaceutical ingredients (API), these dosage forms can achieve a longer gastric residence time (GRT). You can make the medication delivery system float by adding A chamber filled with air that floats, vacuum, or inert gas from the system. The stomach is cleared of any leftover medication after the substance has been released. As a result, there is a greater control over variations in plasma drug concentration and an elevated GRT.[4]

Floating drug delivery systems (FDDS) can stay due to their lower bulk density than gastric fluids, they can remain in the stomach for extended periods of time without affecting the rate of gastric emptying.. The drug is carefully and softly released from the body as it floats on the contents of the stomach. Following the drug's release any leftover medication in the stomach is eliminated. Consequently, variations in plasma drug concentration are better regulated, and the Gastric Residence Time (GRT) is improved. For the system to form a cohesive gel barrier and dissolve gradually enough to serve as a drug reservoir, it must be sufficiently structurally sound to have a specific gravity lower than the total specific gravity of the stomach contents. The techniques for making effervescent and non-effervescent floating tablets based on buoyancy were utilized in the development of FDDS . Medication with a restricted therapeutic window can be administered via the previously indicated practical techniques.[5]

Because they are low density, floating drug delivery devices are intended to carry medications with low intestinal solubility or poor stability into the stomach by floating above the gastric fluid.

The dosage forms are contained in hydroxypropyl cellulose and sodium and citric bicarbonate

tablets., and other gas-producing materials that release carbon dioxide when they come into contact with stomach contents, which helps the tablets float.[6] The long half-life of gastro-retentive dosage forms. which are intended to remain in the stomach and release their active ingredients, enables the upper gastrointestinal system to get consistent, long-term medication delivery. Any medication delivery system should aim to reduce the frequency and intensity of unwanted side effects while simultaneously rapidly achieving and maintaining the optimal therapeutic drug concentration that starts pharmacological activity. This is accomplished by administering a therapeutic dose of the medication to the appropriate body location at the appropriate time.[7]

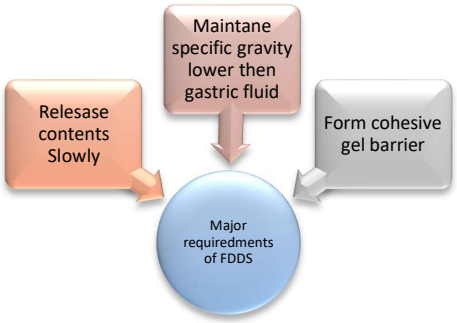


Fig: 1 Requirement of FDDS

Mechanism of Floating of Floating Effervescent Tablet:

When the system is floating on the contents of the stomach, as shown in figure 2, the necessary pace during the system flow on the gastric contents, complements the delayed medication release. After pressure is released, the remaining system is then taken out of the stomach. However, to maintain the dose form buoyant above the meal surface and to accomplish the buoyancy retention principle, minimum amounts of stomach contents are also required in addition to the appropriate amount of floating force (F).. The literature has described a novel method for calculating resultant weight (RW) to evaluate the kinetics of the floating force. Its method of operation is to measure the force that maintains the item submerged and is equal to F (with regard to time). If RW is higher on the positive side, the object floats more effectively (see picture 1(b)).This device maximizes FDDS and mitigates its disadvantages, which include unpredictable intragastric buoyancy capacity fluctuations that affect stability and durability.

RW or F = F buoyancy –F gravity

= (Df–Ds) gV

Where, F= total vertical force,

D_f = fluid density,

Ds= object density,

V = volume and

g = acceleration due to gravity.[8]

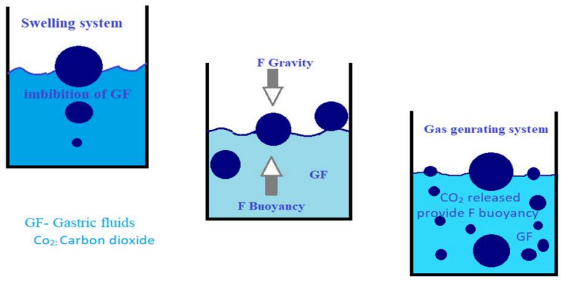


Fig 2 Mechanism of FDDS,

Physiology of Stomach

The dilated, J-shaped stomach is a part of the digestive system. that is situated in the left hypochondriac, umbilical, and epigastric regions of the abdominal cavity. Its size changes according to how much food it holds. Adults have a volume of 1.5 liters or more, and once the food has been consumed, they reach a "collapsed state" when they merely have a 25–30 milliliter resting volume. The body, antrum, and fundus comprise the stomach. A sphincter called the pylorus is located between the duodenum and the most terminal antrum.[9]

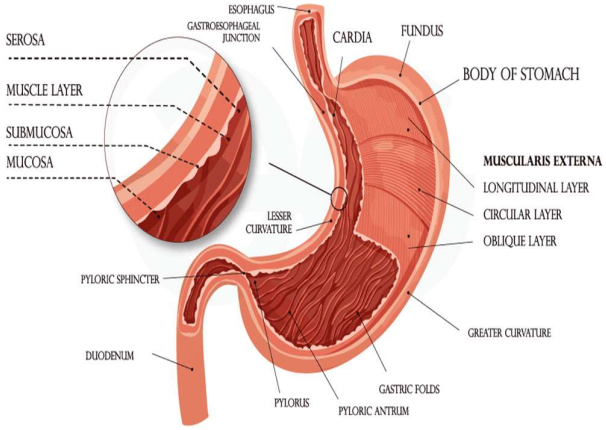


Fig. 3 Stomach anatomy

One organ that is hollow and a part of the digestive system is the stomach. It creates chyme, makes the proteins needed to absorb vitamins, protects against bacteriaas well as initiate the peristaltic reflex. Nutrient absorption does not include the stomach, unlike what the general public believes. The peritoneal cavity, situated in the epigastric abdominal region or the left upper abdomen quadrant, houses this organ, which acts as a conduit for food from the neurological system to the endocrine system

Advantage of Floating Bilayer Tablet (8-9-11)

- The hydrodynamilcally balanced system (HBS) dosage form alters the duration of the gastric residence and allows for prolonged drug delivery because it remains in the stomach foe a few hours
- It upholds the ideal theurapeutics window,which leads to the achievement of controlled release medication administration because of its simplest administration, there is an improvement in patient compliance.
- It consistently keeps blood levels satble.[8]

- When using the single layer conversion kit , bi-layer implementation is taken into conserdation.
- The price of the oral dosage form was more than that of the other dosage forms.
- When compared to alternative dosage forms, chemicals and microrganisms showed higher stability.
- Flexible concept : coating technique were used to mask the odour and unpleasant taste.
- It is the unit dosae form form with reduced content variability and superior dose precion.[9]
- Some medication classes that may be advantageous for the distribution of gastroretentive medicines.

    - Medications that work specifically in the stomach.
    - Medications mostly absorbed in the stomach.
    - Those medications with low absorption in an alkaline pH.
- They are more stable as compared to other oral methods.
- Coating process can cover objectionable smell and harsh taste.
- Provides the least consistent composition and the highest precision.

Disadvantage of Bilayer Floating Tablet

- To ensure that the system floats correctly, the stomach's fluid levels must rise**.**
- It is not feasible to produce drugs with stomach stability or solubility problem.
- Floating dosage forms can not be created for medications that irritate the mucosa in the stomach.
- The main issue with bilayer pills is capping. hardness Is further issue.[8]
- There's a potential that layers will mix.
- Issues with swallowing in the patients who are unconscious or children.
- Insufficient dissolving characteristics and sufficient wetting might lead to bioavailability issues.
- There are sevral variables that can impact gastric retention, including pH, food presence, and stomach motility. It is impossible to predict the buoyancy because these factors are always changing.
- It is not appropriate to formulate drugs that irritate or include lesions to the stomach mucosa as floating drug delivery system.
- A significant amount of variation in how long it takes the stomach to empty completely or partially.

Challenges in Bilayer Manufacturing

In theory Bilayer tablets are essentially a combination of two single-layer tablets. Actually, there are a number of production obstacles..

Delamination: The tablet fractures when its two parts don't stick together completely. When crushed, the two granulations ought to stick together.

Cross-contamination: When the first layer's granulation blends with the second layer's, or vice versa, this is known as cross-contaminatio9n. It might even go against the original design of

the dual-layer tablet. Efficient dust collection is a key component in lowering cross contamination.

Cost: For a number of reasons, bilayer tableting is more expensive than single layer tableting. There are mainly three reasons initially is too much costly press another is machine run slow. Third, it takes more time to design, evaluate, and validate the formulation since two suitable granulations must be established. If these factors are not appropriately managed or altered, they will have an impact on the overall bilayer compression and the bilayer tablets' quality characteristics (sufficient mechanical strength to maintain the tablets' integrity and individual layer weight management). Therefore, understanding the root causes is essential to enabling the development of a resilient process and product.[14]

Factor Affecting on Floating and Floating Time [6,15-16]

Density: A dosage form's density has a significant impact on both its buoyancy and floating efficiency.

Shape of dosage form: The floating potential of devices with ring and tetrahedron shapes is higher than that of other designs. Their retention is 90–98% higher for a 24-hour period.

Single or multiple unit formulation: Multiple unit formulations provide a higher margin of safety against dosage form failure than single unit dosage forms do.[6]

Size: The dose form's size may also have an impact on the duration of gastric retention. It is recommended that the dosage form size not exceed 9.5 mm in diameter, since this may result in an extended stomach retention period.

Frequency of feed: When multiple meals are given instead of only one, the frequency of migrating myoelectric complexes (MMCs) is low, which might cause the stomach retention duration to increases more than 400 minutes.

Gender:. Regardless of weight, height, or body surface area, the mean ambulatory stomach retention time in males is 3.4–0.6 hours or less in relation to their age, and 4.6–1.2 hours in girls of the same race.22

Age: Elderly people over 60 have significantly longer floating times.

Nature of meal: When indigestible polymers are present, the stomach's motility pattern may change to a fed state, or it may be administered fatty acid salts. This may slow down the emptying of the stomach and extend the time that medication is released.

Calorie content: A high-fat, high-protein meal might add four to ten hours to your floating duration.

Biological factor: Floating may differ based on an individual's physiological state or state of health. Floating time is affected, for example, by both Crohn's disease and diabetes.[23]

Techniques of Floating Bilayer Tablet

To produce bilayer tablets of the appropriate quality, a variety of bilayer tablet manufacturing procedures are used The erodible multilayer drug system, (A)En SO TROL Technique,(B) L-OROS Tm technology, (C) DUROS technology, (D) Duredas/Elan drug technology, programmable oral drug absorption system (Prodas), Geomatrix technologies, Geminix technology, and osmotic-release oral system (OROS) push-pull technology are some of the techniques used in this process. These are described with diagrams.

- **EN SO TROL Technology** : An magnitude improvement in soluble form or the development of an ideal dosage form Shire Laboratory employs an integrated medication

delivery strategy that focuses on identifying and integrating the identified booster into technologies with controlled release.[18]

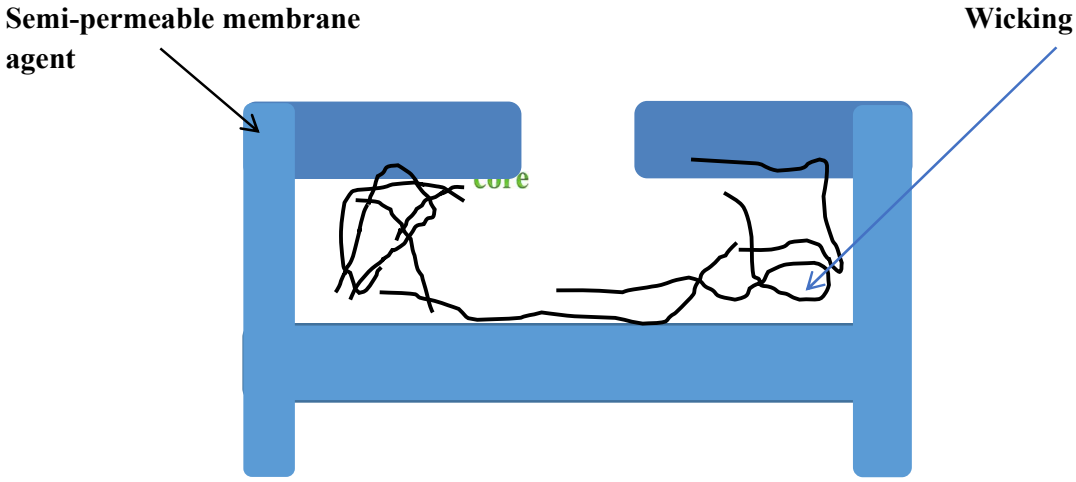


Fig. (4) EN SO TROL Technology

- **OROS push pull technology**: Two or three layers make up the majority of this structure, the remaining levels being push layers and one or more of them being required for the medication. The drug and two or more different agents are the main elements of the drug layer.. employed in the drug layer, including osmotic and suspending agents. The tablet's core is surrounded by a semipermeable membrane[19].

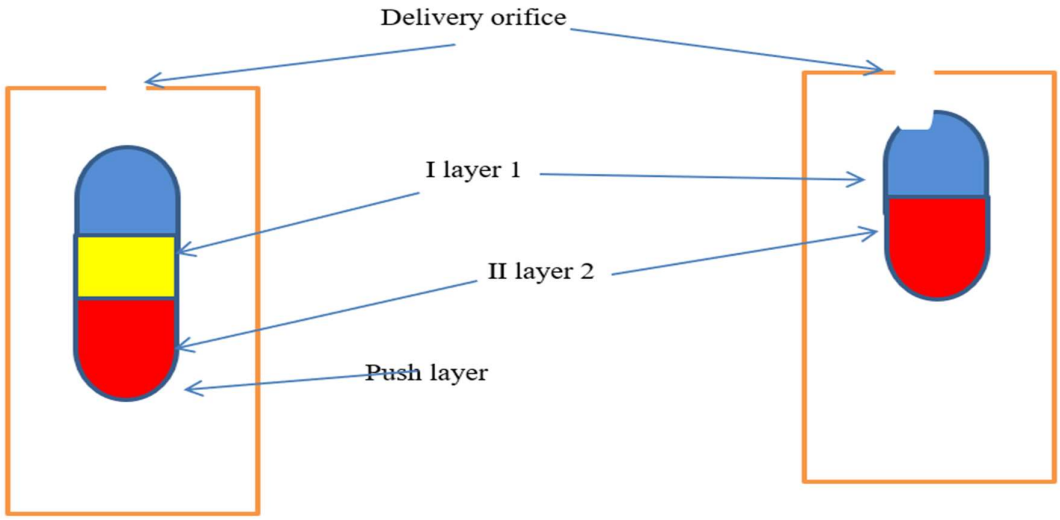


Fig. no. (5) OROS PUSH PULL TECHNOLOGY

- **L-OROS® tm technology**: This approach to the solubility issue Alza created the L-OROS mechanism, It begins with the production of a lipid soft gel product that has a medication dissolved in it. Next, A barrier membrane, an osmotic push layer, a semi-permeable membrane, and an exit aperture are applied to the product in that order.[20]

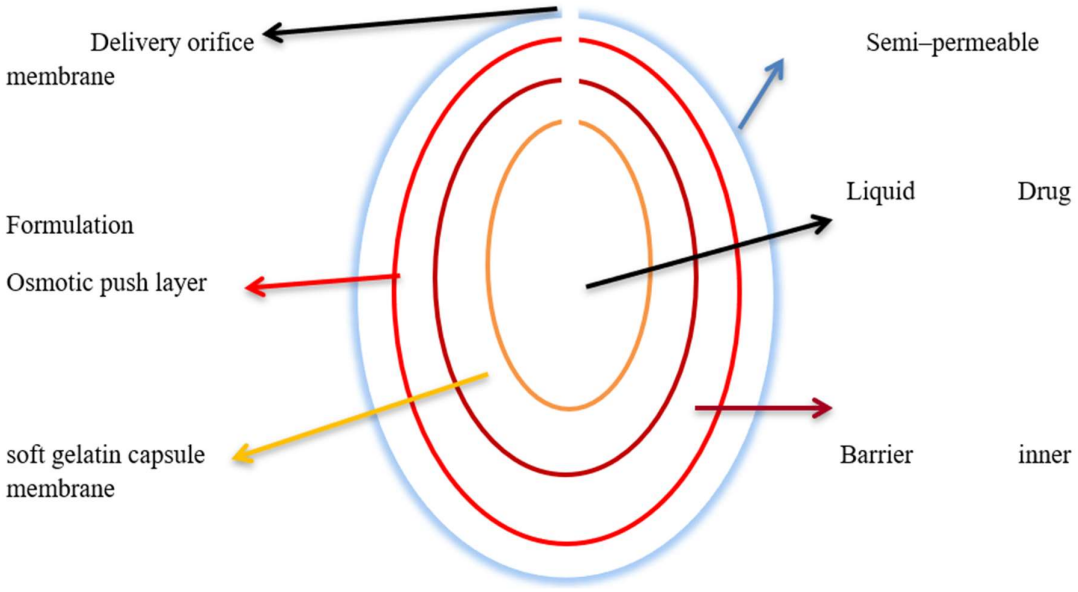


Fig. no. 05 L-OROS® tm Technology

- **DUROS® Technology**: The hub of the system is the external, cylindrical titanium alloy reservoir. This reservoir shields the medication molecules from enzymes and has a high impact strength. Over the course of several months or years, a small amount of concentrated form is continually and consistently released using the device It functions much like a small syringe.[21]

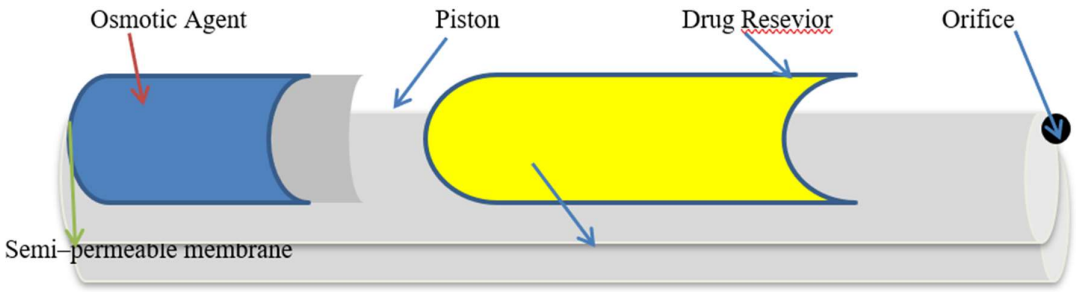
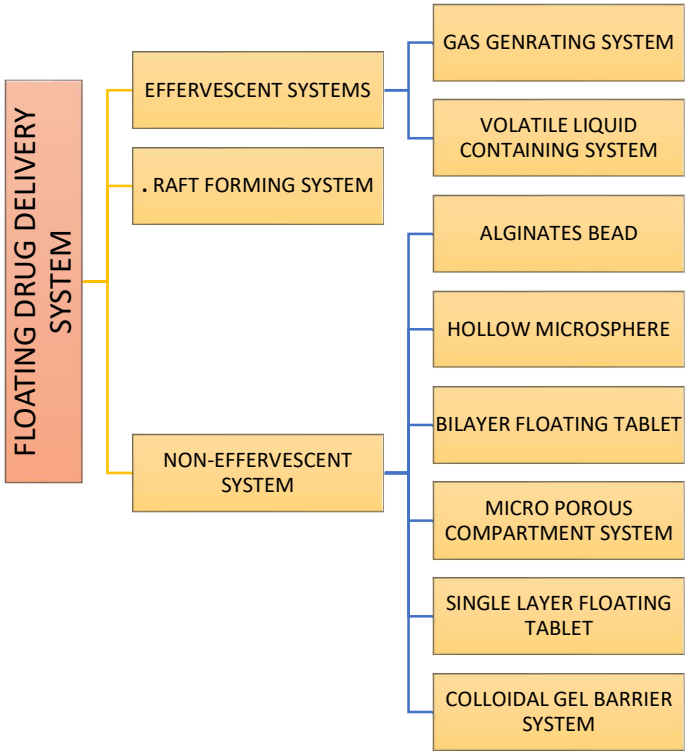


Fig. 5 DUROS® Technology

- **Elan drug technologies:** Two-Phase Drug Administration System With the assistace of DUREDASTM Technology, medications can be released in combination or separately, resulting in both immediate and sustained release patterns. Several controlled release formulations are used together in this.[19]
- **DUREDAS™ technology** : This device is also known as Elan Drug Technologies' Dual Release Drug Delivery device. A bilayer tablet with DUREDASTM Technology can provide two medications at distinct release rates or either instantaneous or sustained release in a single dose form. Within a single tablet, the tableting technique can produce two distinct layers: an updated version hydrophilic matrix combination and an immediate release granulate. A mixture of hydrophilic polymer.[20]

Classification of Floating Drug Delivery System



Flow chart classification of FDDS

A.Effervescent system These systems are matrix-based. made possible by a variety of swellable polymers and effervescent substances, including methylcellulose and chitosan. Examples include tartaric acid, sodium bicarbonate, and citric acid. They are designed in a way that releases carbon dioxide when they come into contact with stomach contents and traps it in expanding hydrocolloid, giving the dosage form buoyancy. The swellable asymmetric triple layer tablet method served as the foundation for the delivery mechanism's design.

1. Gas generating system: These have a minimal density. The production of CO2 is the creation of CO_2 inside the apparatus as a result of bodily fluid contact. The materials are made in such a way that, when CO2 enters the stomach, the acidity of the gastric content librates it, trapping it in the gellified hydrocolloid and causing it to rise and remain buoyant. Dosage shape is suspended on the in specific chime because to a reduction in gravity. The components that produce CO2 can be thoroughly blended with the tablet matrix to create either a single layer or two layers, with the medicine ready for a longer-lasting effect in one layer and the mechanism in the gas generating other hydrocolloid-containing layer.[22]

2. **Volatile liquid containing system:** This gadget is made up of a hollow, deformable module that is in a collapsed state. It is used in an osmotically controlled floating technique. Internally, the housing would be joined to its pliable module and partitioned into a primary and secondary chamber, divided by a movable, impermeable unit that responds to pressure. The drug reservoir can float because The volatile liquid in the second chamber—such as ether or cyclopentane—vaporizes to produce a gas at a temperature equivalent to that of the body. The first chamber

typically holds the active medication. A bioerodible stopper is used to remove the module from the stomach, allowing the vapour to escape.[23]

B.Non-effervescent System: The non-effervescent FDDS is caused by polymer swelling or bioadhesion to the mucosal layer of the gastrointestinal system. Following ingestion, the medication expands in response to the absorption of gastric fluid, obstructing the stomach's ability to empty itself. The medicine is primarily blended with gel, which causes it to retain its shape and swell when it comes into touch with stomach fluid. Given their propensity to become lodged close to the pyloric sphincter, One term for these systems could be "plug-type systems." The hydrocolloids of the gel-forming or highly swellable cellulose type, polysaccharides, and matrix-forming polymers such as polyacrylate, polymethacrylate, and polycarbonate are the most often used excipients in non-effervescent floating drug delivery systems.[24]

1. **Colloidal gel barrier system**: This technique maximum the amount of medication that absorbed from the absorption site and lengthens the stomach retention period. It is composed of medications that, in order to maintain their stomach contents, contain gel-forming hydrocolloids. This system contains hydrocolloid cellulose gel-forming polymers, such as polysaccharides, polycarbophils, polyacrylates, and polyhydroxypropyl methyl cellulose (HPMC), as well as polymers producing matrix. When hydrocolloid comes into contact with the gastro-intestinal (GI) A8-25, it hydrates while creating an environmental gel colloid barrier.

1. **Colloidal gel barrier system**:

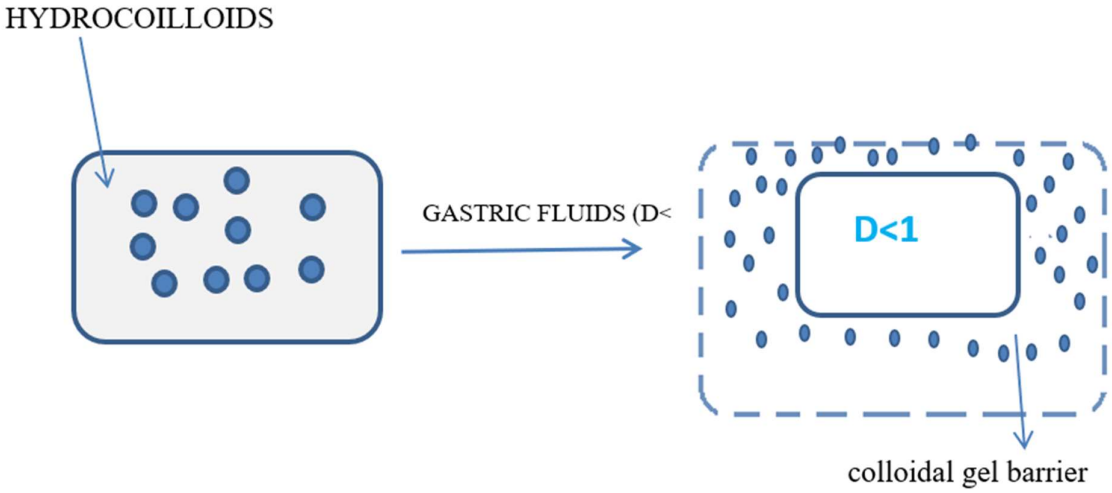


Fig no. 6 colloidal gel barrier system

2. **Intra-gastric / Microporous compartment system** This technique functions by confining a drug reservoir within a microporous compartment with holes in the walls on both the top and bottom. To keep the stomach mucosal surface from being in contact with the undissolved medicine the medication reservoir compartment's outside sides are tightly sealed. The delivery system floats above the contents of the stomach due to the air held in the flotation chamber. The drug dissolves in the stomach juice that enters through the perforations and is constantly transported for absorption through the intestine.[26]

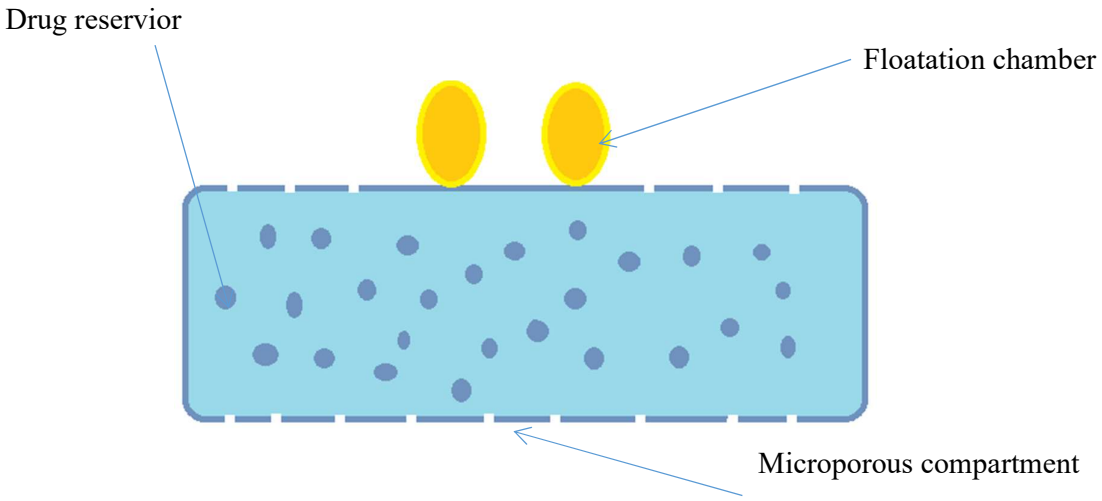


Fig no. 7 microporous compartment

3.Hollow microspheres / Microballons The most efficient buoyant device is believed to be a hollow microsphere, also known as a micro balloon.. It is made up of the microsphere's interior center hollow region Hollow microspheres having a drug within their outer polymer shelf are created using a novel solvent. Method of diffusion for emuls Calcium alginate is freeze-dried to create these dosage forms. The process of making spherical beads involves introducing a sodium alginate solution into a calcium chloride aqueous solution.[27]

4**. Alginate beds**: Calcium alginate precipitates as a result of this. Solid beads and calcium alginate beads were contrasted. The beads were found to be extending the duration of occupancy. The GRT for solid beads was determined to be one hour, while the GRT for calcium alginate beads was discovered to be 5.5 hours.[28]

C. Raft forming system: Here, stomach juice containing trapped CO2 bubbles causes a gel-forming solution to swell and produce a thick cohesive gel. In order to reduce stomach acidity, antacids like calcium carbonate or aluminum hydroxide are frequently employed in formulations. Raft forming systems are also utilized to treat gastro-oesophageal because they create a layer on top of stomach contents, causing reflux. One of the methods via which rafts arise is the formation of a cohesive gel that is viscous when in touch with stomach contents. In each area, the liquid expands to form a continuous layer that is referred to as a raft. Due to the low density and carbon dioxide emissions of stomach contents, this raft floats on them.[24,29]

How The Floating Drug Delivery System is Prepared

Direct compression method :. It uses compression tablets directly out of the powder without altering the physical makeup of the substance. Tricalcium phosphate, dicalcium trihydrate phosphate, etc. are among the most commonly used carriers.

Effervescent technique: Bicarbonate salts and organic acid (citric acid) will react effervescently to produce inert gas (CO2) that will fill the floating chamber of the drug delivery device.

Wet granulation technique includes moistening powder and rubbing, grinding, or drying it.

Effervescent Technique: Bicarbonate salts and organic acid (citric acid) will react effervescently to produce inert gas (CO2) that will fill the floating chamber of the drug delivery device. Rather than compacting the particles, wet granulation forms the granules by binding the powders together with an adhesive.[30]

Ionotropic Gelation Technique: Effervescent Technique: Bicarbonate salts and organic acid (citric acid) will react effervescently to produce inert gas (CO2) that will fill the floating chamber of the drug delivery device.. The propensity to create cross links promotes ionotropic gelation, which becomes beads. when counter-ionic polyelectrolytes are present. This method of gelation has been widely utilized to bead preparations then the adoption of gallon gum, chitosan, alginates, and CMC for drug encapsulation. These anions engage in gelation primarily through their combination with anion chunks, and they create structures resembling meshes by interacting with adaptable cations. If the drug-loaded polymer solution is dropped into a flexible cationic aqueous phase, hydrogel beads are produced.[31]

solvent evaporation technique: It is not possible for a continuous phase to eliminate all of the liquid dispersal solvent.On the dispersal surface, the solvent evaporates to produce hardened microspheres.

Spray drying technique: Effervescent Technique: Bicarbonate salts and organic acid (citric acid) will react effervescently to produce inert gas (CO2) that will fill the floating chamber of the drug delivery device. By quickly evaporating the coating material, the core layer is dispersed throughout the liquid coating content. The coating is then solidified by spraying the core coating mixture into the surrounding area.

Melt solidification technique: Using this procedure, the molten material must first be emulsified in an aqueous phase before being cooled and solidified. This method uses lipids, waxes, polyethylene glycol, and other substances as carriers.

Melt Granulation Technique: This granulation method aggregates medicinal powders without the use of organic solvents or water by using a meltable binder.[32]

Evaluation of Bilayer Floating Tablet

Pre-compression parameters

Effervescent Technique: Bicarbonate salts and organic acid (citric acid) will react effervescently to produce inert gas (CO2) that will fill the floating chamber of the drug delivery device.. The funnel method was used to calculate the granules' angle of repose. The grains were weighed very precisely and collected using a funnel. The funnel's height was changed such that the tip just touched the top of the grain pile Granules were let to escape the funnel and land on the surface without restriction. The following equation was used to calculate the angle of repose after the diameter of the powder cone was measured:

Angle of repose [33]

$$\boldsymbol{Angle\ of\ repose}\ \tan\theta = \frac{h}{r} \quad (1.1)$$

h = Height of the powder cone.

r = Radius of the powder cone

Table 01 Angle of repose and powder flow related to each other

Angle of repose	Powder flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density The volume of powder is measured when a suitable weight of powder is added to the measuring cylinder.[34]

2. $$\boldsymbol{Bulk\ Density} = \frac{\boldsymbol{Weight\ of\ powder}}{\boldsymbol{Volume\ of\ powder}}$$

Tapped density A precisely measured quantity of powder has been added to the bulk density device. Up to the volume plateau, the cylinder was struck every two seconds starting at a height of 2.5 cm. The formula below has been utilized to determine the taped density (t).[35]

:ρt= mV

Compressibility index (CI) / Carr's index[36]

3. $$\%\ \boldsymbol{Carr's\ index} = \left\{\boldsymbol{Tapped\ density} - \frac{\boldsymbol{Bulk\ density}}{\boldsymbol{Tapped\ density}}\right) \times \mathbf{100}$$

Hausner's Ratio: the Tapped density is divided by the Bulk density to determine the result.[36]

3.1 $$\boldsymbol{Hausner's\ Ratio} = \frac{\boldsymbol{Bulk\ density}}{\boldsymbol{tapped\ density}}$$

Table:2 Carr's index and Hausner's Ratio

Flow ability	Carr's index	Hauser's ratio
Excellent	0-10	1.0- 1.11
Good	10-15	1.12- 1.18
Fair	16-20	1.19- 1.25
Possible	21-25	1.26- 1.34
Poor	26-31	1.34- 1.45

Percentage porosity: The calculation's total porosity expression is the same whether the powder is permeable or not. Porosity gives details about things like overall porosity, hardness, and disintegration.[37]

3.2 $$\%\boldsymbol{porosity} = \left(\frac{\boldsymbol{volume\ of voids}}{\boldsymbol{total\ volume}}\right) \boldsymbol{x}\ \mathbf{100\%}$$

3.3 $$\%\ \boldsymbol{porosity} = \left(\frac{\boldsymbol{total\ volume - volume\ of solid}}{\boldsymbol{total\ volume}}\right) \boldsymbol{x}\ \mathbf{100\%}$$

Particle size distribution

Utilizing a sieve technique, the particle size distribution was examined.

Photomicroscope study: Using a photomicroscope 38, an image of TGG and GG was captured at ×450 magnification

Post compression parameter

Disintegration time Each testube disintegration test equipment had one tablet placed within a

beaker filled with buffer (0.1N HCl or phosphate buffer solution with a pH of 6.8) and the test was run at 37°C. Disintegration time is the term used to describe the drug's disintegration period.[39]

IN vitro dissolution studies With the aid of the USP paddle apparatus, the dissolution test was carried out by maintaining a temperature of 37ºC for 50 rpm (rpm) of rotational speed. Following this, 0.5 ml of sample was removed at a different time interval, and the 5 ml solution was substituted with the 5 ml of buffer solution.28[39]

Friability: Friability testing is used to test the durability of tablets during packing processes and transit.

1. 10 tablets are selected,
2. Weighed of tablet
3. placed in Roche friabilator,
4. it spins at 25 rpm speed for four min.
5. Four minutes later, the tablets are weighed again. Friability is calculated using Calculating friability is done using formula,

$$3.4\ \%Weight\ loss = \left(\frac{initial\ weight - final\ weight}{initial\ weight}\right) x\ 100\%$$

Tablet friability is deemed acceptable if it is less than 1%.

Tablet Density: In the case of floating tablets, it is a crucial parameter. The pills will float if the density is lower than the stomach fluid (1.004). It is computed using the formula that follows.[40]

Density = weight of tablet/ Volume of tablet

v= volume of tablet in ml

m= mass of tablet in gm

Buoyancy / Floating test

The pills were put into a 250 mL beaker along with 200 mL of 0.1 N HCl. [37]. The dosage form was given, and the amount of time that elapsed before it began to float in the simulated stomach fluid was measured. Total Floating Time (TFT) measures how long the dosage form remains buoyant.[41]

Hardness Test: The tablet needs to be the right hardness to withstand mechanical pressures during manufacturing, handling, shipping, and storage. A Langen, Germany-based Erweka TB 24 device was used to measure each formulation's hardness.

For each batch, a random sample of five tablets was taken to determine the hardness. Following was the computation of the gathered values: mean ± SD42 [42]

Weight variation test:[43] From each formulation, twenty pills were chosen at random, average weight was considered. Each tablet was weighed separately and the results were compared to the average weight. A slight variance in a tablet's weight is permitted by the US Pharmacopoeia.[43]

Dimensions/tablet thickness: Three tablets are measured for thickness and diameter using random calibration of screw gauze or Vernier caliper.[44]

Assay/drug content: Ten randomly chosen tablets containing 100 mg of verapamil HCl were weighed, triturated, and then placed in a 100 ml volumetric flask to dissolve in 0.1N HCl. After 30 minutes of sonication, a 0.45µm membrane filter was used to filter it. Following the appropriate dilutions, 0.1N HCl was used as a blank 44 and the absorbance was measured at

278 nm in a UV Visible Spectrophotometer.[45]

In vivo evaluation Radiology [45]

X-rays are frequently utilized to examine interior body systems. One popular type of radio opaque marker is barium sulphate. In order to observe stomach retention, BaSO4 is integrated into the dose form and X-ray images are obtained at different intervals.[45]

Gastroscopy: The method used to visually evaluate the effects of extension in the stomach is called gastroscopy. Additionally, it can provide a thorough assessment of the GRDDS.
Ultrasonography utilized infrequently; not frequently utilized since it cannot be tracked at the intestinal level
Magnetic marker monitoring By filling the dose form with iron powder, this method first identifies it magnetically. Then, the highly sensitive bio-magnetic measurement equipment may take pictures. The benefit of this approach is that it produces fewer radiation emissions, making it safe for human usage.

Application of floating bilyer tablet

Increased bioavailability: The bioavailability of riboflavin CR-GRDF is significantly higher than that of non-GRDF CR polymeric formulations. The amount of medicine absorbed is influenced by a complex interplay of factors, including drug absorption and transit in the gastrointestinal tract.

Sustained drug delivery Oral Control There have been documented releases from preparations and problems with stomach residence time in the GIT. HBS systems can solve these problems since they can stay in the stomach for extended periods of time and have the bulk density1 required to float on top of the stomach's contents. These bigger gadgets aren't able to fit via the pyloric aperture.[46]
Decreased adverse effects in the colon: With HBS, less medication enters the colon since the medication is kept in the stomach. Consequently, it is possible to stop undesirable drug activity in the colon.

Decreased variations in concentration at the medication: A narrower range of blood drug concentrations is achieved with continuous drug input following CR-GRDF delivery compared to other types of instant release dosage forms.[47]

Systems for site-specific drug delivery:[48]
For medications that are primarily absorbed in the proximal small intestine or stomach, these systems are quite helpful. While minimizing the drug's systemic exposure, the medication is delivered to the stomach gradually and under observation to guarantee adequate local therapeutic levels. As a result, the drug's adverse effects on the blood supply are reduced. Furthermore, the extended stomach availability of a site-guided administration device can

lower the frequency of dose. Take riboflavin with furosemide, for example

Absorption enhancement

In order to enhance absorption, medication with restricted bioavailability from site-specific absorption from the upper GIT may be prepared as FDDS.[48]

Table: 3 Polymers used in floating drug delivery systems

Tablet	Capsule	Microspheres Microparticulates
Cellulosic hydrocolloids	Cellulosic	Cellulose derivatives
Hydroxypropyl methylcellulose(HPMC)	Hydro colloids	Ethyl cellulode
Methylcellulose	Hydroxypropyl Cellulose (HPC)	
Sodium Carboxymethyl cellulose (CMC)	Hydroxyethyl cellulose (HEC)	
Carabpol	Gel forming hydrocolloids	Eudragit
Carragenan	Sod. Alginate	Polycarbonates
Gum guar	Carbapol	Polyacrylate
Gum Arabic	Agar	Poly methacrylates
Sodium alginate		Poly styrene
Poly ethyelene oxides		Chitosan
Polyvinyl lactam		Gelatin
Poly acryalates		Alginates
Polyvinyl aceatate		Gelucir

There are following recent work on floating drug delivery systems[49-68].

Table: 4 Recent work on floating bilayer tablet

Sr no	Drug name	Types of tablet	Excipient or polymer	Disease or disorder	Method
1	Losartan Hydrochlorothiazide	Floating bilayer tablets	HPMC K4M	Anti-hypertension	Direct compression method
2	clarithromycin and esomeprazole,	Floating bilayer tablets	Sodium bicarbonate	*Helicobacter pylori* infection	Direct compression method.
3	Losartan Potassium, Ramipril Hydrochloride	Gastro-Bilayer Floating matrix	Hpmc, Sodium bicarbonate, Citric acid	chronic hypertension	Direct compression method

		Tablets,			
4	Clarithromycin, Famotidine	Floating bilayer tablets	HPMC K100M HPMC K4M SODIUM Bicaronate	*Helicobacter pylori* infection	Direct compression method
5	Nateglinide, Atenolol	Biphasic Gastro Floating Tablets	HPMC K15, SODIUM BICARBONATE, MCC	Anti-hypertensive, Antidiabetics	Direct compression method
6	Metoprolol tartarate indapamide hemihydrate	BILAYER Tablet	HPMC K100M HPMC K4M SODIUM Bicaronate Pvp k-30	Anti-hypertensive	Direct compression method
7	Clarithromycin, pantoprazole	Gastro-retentive floating bilayer tablet	HPMC K15M	*Helicobacter pylori* infection	Direct compression method
8[56]	ketorolac tromethamine	Gastro retentive bilayer tablet	Ac-di-sol, Sodium bicarbonate, HPMC K100M, HPMCK4M	Anti-infammatory and analgesic	Rotary punching tablet machine
9	Aceclofenac, esomeprazole	bilayer floating tablet	HPMC E15, HPMC K100M, HPMC E5	analgesics, NSAIDS	Direct compression method
10	Nicardipine	Bilayer tablet	Sodium starch glycolate, MCC, PVP K3	antihypertensive	Direct compression method (stationary double rotary compressio)
11[59]	Epleronone	Floating bilayer tablet	MCC, Sodium bicarbonate , Pvp k30 citric acid	antihypertensive	Direct compression method
12[60]	Repaglinide, glipizide,	Floating bilayer tablet	Hydroxypropyl Methylcellulose K4M, Sodium Carboxymethyl	Type 2 diabetes	Direct compression method

			Cellulose, Microcrystalline Cellulose, Polyvinyl Pyrilidone (PVP K30), SLS , PVP K30, $NAHCO_3$, Mg sterate, citric acid		
13	Levofloxacin, Famotidine	Control release bilayer floating effervescent and non-effervescent tablets	HPMC K4, HPMC K15, HPMC K100,	Ani ulcer	Direct compression method
14	Metoprolol Succinate	Floating bilayer tablet	HPMC K100M, SODIUM Bicarbonate , Ethyl celluloe	Hypertension, Pregnancy & lactation.	Direct compression method
15	Amlodipine hydrochlorothiazide	Gastro-retentieve bilayer floating tablet	Sodium starch glycolate , PVP K30 , HPMC K 100 M Sodium bicarbonate	Hypertension	Direct compression method
16	Ramipril Hydrochloride	Floating matrix bilayer tablet	HPMC K100 , CARBOPOL, PVP K30.	hypertension	Direct compression method
17	Diltiazem hydrochloride	Floating bilayer tablet	HPMC K4M, K15M, PVP K30	Hypertension and angina	Direct compression method
18	Esomeprazole, Levosulpiride,	Bilayer tablet	Croscarmellose sodium, Sodium Starch glycolate, HPMC K4, HPMC K15, PVP K30	Anti ulcer	Direct compression method
19	Bosentan	Floating	HPMC K4M, E-	Hypertension	Direct

		bilayer tablet	15		compression method
20	Lansoprazole, Amoxycillin	bilayer tablet	HPMC , K100M, PVP K30	ANTIULCER	Direct compression method

Conclusion:

In conclusion, the upper GIT is possibly the best location of the GI tract for absorption of orally administered drugs with poor bioavailability, and FDDS (GRDDS) would be an excellent way to provide drugs whose extent of absorption is restricted to the upper GIT, thereby causing these drugs to be a good target for delivery in the upper GIT as a specific absorption window – localized GRDDS . The development and application of floating tablets in the treatment of peptic ulcers are of great value to the clinical treatment and the life quality of patients, and at the same time, it is obvious that different bilayer tablets can produce altered APIs for combination therapy at present, or the same API can be administered with an initial loading dose, followed by maintenance dose in order to maintain the effective pharmacological activity in plasma for an adequate period of time.

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